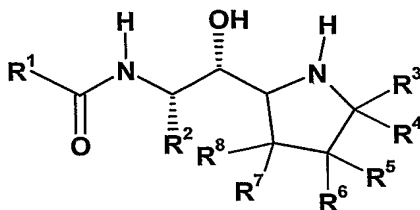


We Claim:

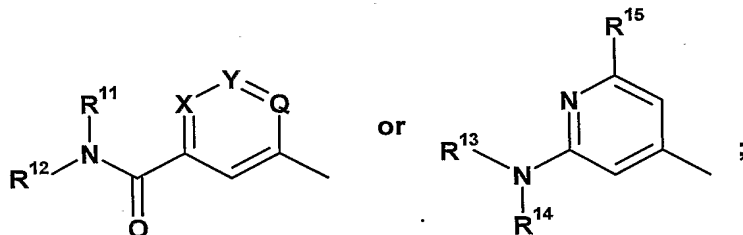
1. A compound of Formula I:



I

where:

R<sup>1</sup> is (C<sub>3</sub>-C<sub>7</sub> cycloalkyl)<sub>0-1</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), (C<sub>3</sub>-C<sub>7</sub> cycloalkyl)<sub>0-1</sub>(C<sub>2</sub>-C<sub>6</sub> alkenyl), (C<sub>3</sub>-C<sub>7</sub> cycloalkyl)<sub>0-1</sub>(C<sub>2</sub>-C<sub>6</sub> alkynyl) or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, each optionally substituted with up to three groups independently selected from halo, hydroxy, thiol, cyano, trifluoromethyl, trifluoromethoxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>3</sub>-C<sub>7</sub> cycloalkoxy, oxo, and NR<sup>9</sup>R<sup>10</sup>, hydrogen,



biphenyl substituted with halo,

X is CH, N, or N<sup>+</sup>-O<sup>-</sup>;

Y is CR<sup>16</sup>, N, or N<sup>+</sup>-O<sup>-</sup>;

Q is CR<sup>17</sup>, N, or N<sup>+</sup>-O<sup>-</sup>;

R<sup>2</sup> is C<sub>1</sub>-C<sub>3</sub> alkyl, benzyl optionally monosubstituted in the phenyl ring with a substituent selected from the group consisting of halo, C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted in the alkyl chain with C<sub>3</sub>-C<sub>7</sub> cycloalkyl, and C<sub>1</sub>-C<sub>6</sub> alkylthio optionally substituted in the alkyl chain with C<sub>3</sub>-C<sub>7</sub> cycloalkyl, or benzyl optionally disubstituted in the phenyl ring with a first substituent independently selected from halo and a second substituent independently selected from halo, C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted in the alkyl chain with C<sub>3</sub>-C<sub>7</sub> cycloalkyl, and C<sub>1</sub>-C<sub>6</sub> alkylthio optionally substituted in the alkyl chain with C<sub>3</sub>-C<sub>7</sub> cycloalkyl;

R<sup>3</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sup>4</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, or phenyl;

$R^3$  and  $R^4$  taken together with the carbon to which they are attached form a  $C_3$ - $C_6$  cycloalkyl ring;

$R^5$  is hydrogen, fluoro, trifluoromethyl,  $R^{32}$ , or phenyl optionally monosubstituted with  $C_1$ - $C_6$  alkyl or  $C_1$ - $C_6$  alkoxy;

5  $R^6$  is fluoro, hydroxy, *p*-toluenesulfonyloxy,  $R^{34}$ ,  $-\text{CH}_2\text{C}(\text{O})\text{R}^{35}$ , or  $-\text{OC}(\text{O})\text{NHR}^{36}$ ; or  $R^5$  and  $R^6$  taken together form  $=\text{CHC}(\text{O})(\text{C}_1\text{-C}_4 \text{ alkoxy})$ ;

$R^7$  is hydrogen or fluoro; or  $R^6$  and  $R^7$  taken together form a bond;

$R^8$  is hydrogen or fluoro;

$R^9$  is hydrogen,  $C_1$ - $C_6$  alkyl, or phenyl;

10  $R^{10}$  is hydrogen,  $C_1$ - $C_6$  alkyl, phenyl,  $-\text{C}(\text{O})(\text{C}_1\text{-C}_6 \text{ alkyl})$ , or  $-\text{SO}_2(\text{C}_1\text{-C}_6 \text{ alkyl})$ ;

$R^{11}$  and  $R^{12}$  are independently selected from the group consisting of methyl, ethyl, and propyl;

$R^{13}$  is hydrogen or  $C_1$ - $C_6$  alkyl;

$R^{14}$  is  $C_3$ - $C_5$  cycloalkyl,  $C_1$ - $C_6$  alkyl, or  $-\text{CH}_2\text{R}^{18}$ ;

15  $R^{15}$  is  $-\text{CF}_2\text{R}^{19}$ ,  $-\text{OR}^{20}$ ,  $-\text{CH}_2\text{C}(\text{O})\text{CH}_3$ ,  $-\text{S}(\text{O})_{1-2}\text{R}^{21}$ ,  $-\text{NR}^{22}\text{SO}_2\text{R}^{23}$ , ( $C_1$ - $C_3$  alkoxy)-carbonyl, phenyl optionally substituted with halo, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,1-dioxo-2,3,4,5-tetrahydroisothiazol-2-yl, or tetrazol-5-yl optionally substituted with  $C_1$ - $C_3$  alkyl;

20  $R^{16}$  is hydrogen, chloro, isobutyl,  $\text{CH}_2\text{R}^{24}$ ,  $\text{CF}_2\text{R}^{25}$ , 1,1,1-trifluoro-2-hydroxyeth-2-yl,  $C_2$ - $C_4$  alkenyl optionally substituted with one or two fluorine atoms,  $\text{OR}^{26}$ ,  $\text{C}(\text{O})\text{R}^{27}$ , N(methyl)(methylsulfonyl), N(methyl)(acetyl), pyrrolidin-2-on-1-yl, methylsulfonyl, N,N-dimethylaminosulfonyl, phenyl optionally substituted with one or two substituents selected from the group consisting of hydroxymethyl, methoxy, fluoro, and methylsulfonyl, 1,3-dioxolan-2-yl, 1,3-dithiolan-2-yl, 1,3-oxathiolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithian-2-yl, pyridinyl, thiazolyl, oxazolyl, or 1,2,4-oxadiazolyl optionally substituted with methyl;

$R^{17}$  is hydrogen or fluoro;

$R^{18}$  is ethynyl or cyclopropyl;

$R^{19}$  is hydrogen or methyl;

30  $R^{20}$  is difluoromethyl or methanesulfonyl;

$R^{21}$  is  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  cycloalkyl, phenyl, or  $-\text{NR}^{30}\text{R}^{31}$ ;

R<sup>22</sup> is hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl optionally substituted with up to 3 fluorine atoms, or C<sub>3</sub>-C<sub>6</sub> cycloalkyl;

R<sup>23</sup> is C<sub>1</sub>-C<sub>3</sub> alkyl or C<sub>3</sub>-C<sub>6</sub> cycloalkyl;

R<sup>24</sup> is fluoro, hydroxy, or C<sub>1</sub>-C<sub>3</sub> alkoxy;

5 R<sup>25</sup> is hydrogen, phenyl, or furyl;

R<sup>26</sup> is C<sub>1</sub>-C<sub>3</sub> alkyl optionally substituted with one or two fluorine atoms;

R<sup>27</sup> is C<sub>1</sub>-C<sub>3</sub> alkyl, C<sub>3</sub>-C<sub>5</sub> cycloalkyl, C<sub>2</sub>-C<sub>3</sub> alkenyl, C<sub>1</sub>-C<sub>3</sub> alkoxy, NR<sup>28</sup>R<sup>29</sup>, pyrrolidin-1-yl optionally substituted with methyl or one or two fluorine atoms, piperidin-1-yl, phenyl, pyridinyl, or furyl;

10 R<sup>28</sup> is hydrogen or methyl;

R<sup>29</sup> is methyl, ethyl, or propyl;

R<sup>30</sup> is hydrogen or methyl;

R<sup>31</sup> is methyl; or

15 R<sup>30</sup> and R<sup>31</sup> taken together with the nitrogen atom to which they are attached form a pyrrolidine or piperidine ring;

R<sup>32</sup> is C<sub>1</sub>-C<sub>10</sub> alkyl optionally substituted with 1-6 fluorine atoms, oxo, or one or two hydroxy groups, C<sub>2</sub>-C<sub>6</sub> alkenyl, or -(CH<sub>2</sub>)<sub>0-3</sub>-R<sup>33</sup>;

20 R<sup>33</sup> is C<sub>3</sub>-C<sub>7</sub> cycloalkyl or phenyl each optionally substituted with one or two substituents independently selected from the group consisting of halo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, hydroxy, trifluoromethyl, and trifluoromethoxy, or R<sup>33</sup> is adamantyl;

R<sup>34</sup> is hydrogen, R<sup>32</sup>, or -(CH<sub>2</sub>)<sub>0-2</sub>-OR<sup>32</sup>;

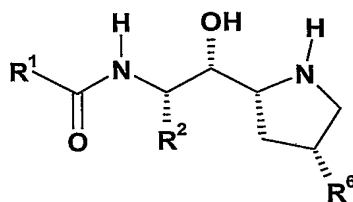
25 R<sup>35</sup> is hydroxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, or NR<sup>37</sup>R<sup>38</sup> where R<sup>37</sup> and R<sup>38</sup> are independently hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl, or R<sup>37</sup> and R<sup>38</sup>, taken together with the nitrogen to which they are attached, form a piperidine ring optionally substituted with C<sub>1</sub>-C<sub>6</sub> alkyl, a homopiperidine ring, a morpholine ring, or a pyrrolidine ring optionally substituted with (C<sub>1</sub>-C<sub>6</sub> alkoxy)methyl;

R<sup>36</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl or adamantyl;

30 or a pharmaceutically acceptable salt thereof; provided that: a) no more than one of X, Y, and Q may be N or N<sup>+</sup>-O<sup>-</sup>; and b) when X is CH, Y is CR<sup>16</sup>, and Q is CR<sup>17</sup>, then one of R<sup>16</sup> and R<sup>17</sup> is other than hydrogen.

2. A compound of Formula I(a):

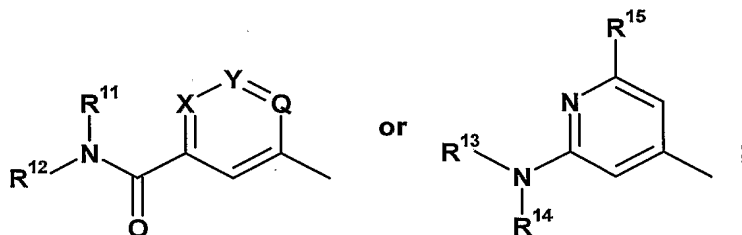
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I(a)

where:

$R^1$  is (C<sub>3</sub>-C<sub>7</sub> cycloalkyl)<sub>0-1</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), (C<sub>3</sub>-C<sub>7</sub> cycloalkyl)<sub>0-1</sub>(C<sub>2</sub>-C<sub>6</sub> alkenyl), (C<sub>3</sub>-C<sub>7</sub> cycloalkyl)<sub>0-1</sub>(C<sub>2</sub>-C<sub>6</sub> alkynyl) or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, each optionally substituted with up to three groups independently selected from halo, hydroxy, thiol, cyano, trifluoromethyl, trifluoromethoxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>3</sub>-C<sub>7</sub> cycloalkoxy, oxo, and NR<sup>9</sup>R<sup>10</sup>, hydrogen,



biphenyl substituted with halo,

X is CH, N, or N<sup>+</sup>-O<sup>-</sup>;

Y is CR<sup>16</sup>, N, or N<sup>+</sup>-O<sup>-</sup>;

Q is CR<sup>17</sup>, N, or N<sup>+</sup>-O<sup>-</sup>;

$R^2$  is C<sub>1</sub>-C<sub>3</sub> alkyl, benzyl optionally monosubstituted in the phenyl ring with a substituent selected from the group consisting of halo, C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted in the alkyl chain with C<sub>3</sub>-C<sub>7</sub> cycloalkyl, and C<sub>1</sub>-C<sub>6</sub> alkylthio optionally substituted in the alkyl chain with C<sub>3</sub>-C<sub>7</sub> cycloalkyl, or benzyl optionally disubstituted in the phenyl ring with a first substituent independently selected from halo and a second substituent independently selected from halo, C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted in the alkyl chain with C<sub>3</sub>-C<sub>7</sub> cycloalkyl, and C<sub>1</sub>-C<sub>6</sub> alkylthio optionally substituted in the alkyl chain with C<sub>3</sub>-C<sub>7</sub> cycloalkyl;

$R^6$  is fluoro, hydroxy, p-toluenesulfonyloxy, R<sup>34</sup>, -CH<sub>2</sub>C(O)R<sup>35</sup>, or -OC(O)NHR<sup>36</sup>; or R<sup>5</sup> and R<sup>6</sup> taken together form =CHC(O)(C<sub>1</sub>-C<sub>4</sub> alkoxy);

R<sup>9</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, or phenyl;

R<sup>10</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl, -C(O)(C<sub>1</sub>-C<sub>6</sub> alkyl), or -SO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl);

$R^{11}$  and  $R^{12}$  are independently selected from the group consisting of methyl, ethyl, and propyl;

$R^{13}$  is hydrogen or  $C_1$ - $C_6$  alkyl;

$R^{14}$  is  $C_3$ - $C_5$  cycloalkyl,  $C_1$ - $C_6$  alkyl, or  $-CH_2R^{18}$ ;

5  $R^{15}$  is  $-CF_2R^{19}$ ,  $-OR^{20}$ ,  $-CH_2C(O)CH_3$ ,  $-S(O)_{1-2}R^{21}$ ,  $-NR^{22}SO_2R^{23}$ , ( $C_1$ - $C_3$  alkoxy)-carbonyl, phenyl optionally substituted with halo, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,1-dioxo-2,3,4,5-tetrahydroisothiazol-2-yl, or tetrazol-5-yl optionally substituted with  $C_1$ - $C_3$  alkyl;

$R^{16}$  is hydrogen, chloro, isobutyl,  $CH_2R^{24}$ ,  $CF_2R^{25}$ , 1,1,1-trifluoro-2-hydroxyeth-2-yl,  $C_2$ - $C_4$  alkenyl optionally substituted with one or two fluorine atoms,  $OR^{26}$ ,  $C(O)R^{27}$ , N(methyl)(methylsulfonyl), N(methyl)(acetyl), pyrrolidin-2-on-1-yl, methylsulfonyl, N,N-dimethylaminosulfonyl, phenyl optionally substituted with one or two substituents selected from the group consisting of hydroxymethyl, methoxy, fluoro, and methylsulfonyl, 1,3-dioxolan-2-yl, 1,3-dithiolan-2-yl, 1,3-oxathiolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithian-2-yl, pyridinyl, thiazolyl, oxazolyl, or 1,2,4-oxadiazolyl optionally substituted with methyl;

$R^{17}$  is hydrogen or fluoro;

$R^{18}$  is ethynyl or cyclopropyl;

$R^{19}$  is hydrogen or methyl;

20  $R^{20}$  is difluoromethyl or methanesulfonyl;

$R^{21}$  is  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  cycloalkyl, phenyl, or  $-NR^{30}R^{31}$ ;

$R^{22}$  is hydrogen,  $C_1$ - $C_3$  alkyl optionally substituted with up to 3 fluorine atoms, or  $C_3$ - $C_6$  cycloalkyl;

$R^{23}$  is  $C_1$ - $C_3$  alkyl or  $C_3$ - $C_6$  cycloalkyl;

25  $R^{24}$  is fluoro, hydroxy, or  $C_1$ - $C_3$  alkoxy;

$R^{25}$  is hydrogen, phenyl, or furyl;

$R^{26}$  is  $C_1$ - $C_3$  alkyl optionally substituted with one or two fluorine atoms;

$R^{27}$  is  $C_1$ - $C_3$  alkyl,  $C_3$ - $C_5$  cycloalkyl,  $C_2$ - $C_3$  alkenyl,  $C_1$ - $C_3$  alkoxy,  $NR^{28}R^{29}$ , pyrrolidin-1-yl optionally substituted with methyl or one or two fluorine atoms, piperidin-1-yl, phenyl, pyridinyl, or furyl;

$R^{28}$  is hydrogen or methyl;

$R^{29}$  is methyl, ethyl, or propyl;

$R^{30}$  is hydrogen or methyl;

$R^{31}$  is methyl; or

$R^{30}$  and  $R^{31}$  taken together with the nitrogen atom to which they are attached form a pyrrolidine or piperidine ring;

5  $R^{32}$  is  $C_1$ - $C_{10}$  alkyl optionally substituted with 1-6 fluorine atoms, oxo, or one or two hydroxy groups,  $C_2$ - $C_6$  alkenyl, or  $-(CH_2)_{0-3}-R^{33}$ ;

$R^{33}$  is  $C_3$ - $C_7$  cycloalkyl or phenyl each optionally substituted with one or two substituents independently selected from the group consisting of halo,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, hydroxy, trifluoromethyl, and trifluoromethoxy, or  $R^{33}$  is adamantyl;

10  $R^{34}$  is hydrogen,  $R^{32}$ , or  $-(CH_2)_{0-2}-OR^{32}$ ;

$R^{35}$  is hydroxy,  $C_1$ - $C_6$  alkoxy, or  $NR^{37}R^{38}$  where  $R^{37}$  and  $R^{38}$  are independently hydrogen or  $C_1$ - $C_6$  alkyl, or  $R^{37}$  and  $R^{38}$ , taken together with the nitrogen to which they are attached, form a piperidine ring optionally substituted with  $C_1$ - $C_6$  alkyl, a homopiperidine ring, a morpholine ring, or a pyrrolidine ring optionally substituted with  
15  $(C_1$ - $C_6$  alkoxy)methyl;

$R^{36}$  is  $C_1$ - $C_6$  alkyl or adamantyl;

or a pharmaceutically acceptable salt thereof; provided that: a) no more than one of X, Y, and Q may be N or  $N^+-O^-$ ; and b) when X is CH, Y is  $CR^{16}$ , and Q is  $CR^{17}$ , then one of  $R^{16}$  and  $R^{17}$  is other than hydrogen.

20

3. The use of a compound of either of Claims 1 or 2 for the manufacture of a medicament for the treatment of Alzheimer's disease.

4. The use of a compound of either of Claims 1 or 2 for the manufacture of a  
25 medicament for the prevention of the progression of mild cognitive impairment to Alzheimer's disease.

5. The use of a compound of either of Claims 1 or 2 for the manufacture of a medicament for the inhibition of BACE.

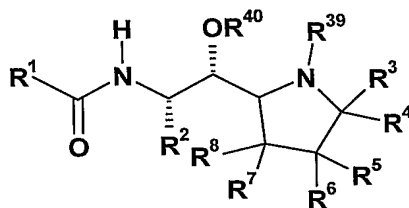
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6. The use of a compound of either of Claims 1 or 2 for the manufacture of a medicament for treating a disease or condition capable of being improved or prevented by inhibition of BACE.

7. A pharmaceutical formulation adapted for the treatment of conditions resulting from excessive levels of A- $\beta$  peptide comprising a compound of either of Claims 1 or 2 in combination with one or more pharmaceutically acceptable excipients, carriers, or diluents.

8. A pharmaceutical formulation comprising a compound of either of Claims 1 or 2, in combination with a pharmaceutically acceptable carrier, diluent, or excipient.

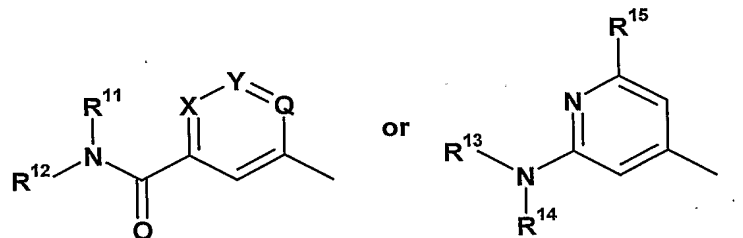
9. A compound of Formula III:



III

where:

R<sup>1</sup> is (C<sub>3</sub>-C<sub>7</sub> cycloalkyl)<sub>0-1</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), (C<sub>3</sub>-C<sub>7</sub> cycloalkyl)<sub>0-1</sub>(C<sub>2</sub>-C<sub>6</sub> alkenyl), (C<sub>3</sub>-C<sub>7</sub> cycloalkyl)<sub>0-1</sub>(C<sub>2</sub>-C<sub>6</sub> alkynyl) or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, each optionally substituted with up to three groups independently selected from halo, hydroxy, thiol, cyano, trifluoromethyl, trifluoromethoxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>3</sub>-C<sub>7</sub> cycloalkoxy, oxo, and NR<sup>9</sup>R<sup>10</sup>, hydrogen,



biphenyl substituted with halo,

X is CH, N, or N<sup>+</sup>-O<sup>-</sup>;

Y is CR<sup>16</sup>, N, or N<sup>+</sup>-O<sup>-</sup>;

Q is CR<sup>17</sup>, N, or N<sup>+</sup>-O<sup>-</sup>;

$R^2$  is  $C_1$ - $C_3$  alkyl, benzyl optionally monosubstituted in the phenyl ring with a substituent selected from the group consisting of halo,  $C_1$ - $C_6$  alkoxy optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, and  $C_1$ - $C_6$  alkylthio optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, or benzyl optionally disubstituted in the phenyl ring  
 5 with a first substituent independently selected from halo and a second substituent independently selected from halo,  $C_1$ - $C_6$  alkoxy optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, and  $C_1$ - $C_6$  alkylthio optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl;

$R^3$  is hydrogen or  $C_1$ - $C_6$  alkyl;

10  $R^4$  is hydrogen,  $C_1$ - $C_6$  alkyl, or phenyl;

$R^3$  and  $R^4$  taken together with the carbon to which they are attached form a  $C_3$ - $C_6$  cycloalkyl ring;

$R^5$  is hydrogen, fluoro, trifluoromethyl,  $R^{32}$ , or phenyl optionally monosubstituted with  $C_1$ - $C_6$  alkyl or  $C_1$ - $C_6$  alkoxy;

15  $R^6$  is fluoro, hydroxy, *p*-toluenesulfonyloxy,  $R^{34}$ ,  $-\text{CH}_2\text{C}(\text{O})\text{R}^{35}$ , or  $-\text{OC}(\text{O})\text{NHR}^{36}$ ; or  $R^5$  and  $R^6$  taken together form  $=\text{CHC}(\text{O})(\text{C}_1\text{-C}_4\text{ alkoxy})$ ;

$R^7$  is hydrogen or fluoro; or  $R^6$  and  $R^7$  taken together form a bond;

$R^8$  is hydrogen or fluoro;

$R^9$  is hydrogen,  $C_1$ - $C_6$  alkyl, or phenyl;

20  $R^{10}$  is hydrogen,  $C_1$ - $C_6$  alkyl, phenyl,  $-\text{C}(\text{O})(\text{C}_1\text{-C}_6\text{ alkyl})$ , or  $-\text{SO}_2(\text{C}_1\text{-C}_6\text{ alkyl})$ ;

$R^{11}$  and  $R^{12}$  are independently selected from the group consisting of methyl, ethyl, and propyl;

$R^{13}$  is hydrogen or  $C_1$ - $C_6$  alkyl;

$R^{14}$  is  $C_3$ - $C_5$  cycloalkyl,  $C_1$ - $C_6$  alkyl, or  $-\text{CH}_2\text{R}^{18}$ ;

25  $R^{15}$  is  $-\text{CF}_2\text{R}^{19}$ ,  $-\text{OR}^{20}$ ,  $-\text{CH}_2\text{C}(\text{O})\text{CH}_3$ ,  $-\text{S}(\text{O})_{1-2}\text{R}^{21}$ ,  $-\text{NR}^{22}\text{SO}_2\text{R}^{23}$ ,  $(\text{C}_1\text{-C}_3\text{ alkoxy})$ -carbonyl, phenyl optionally substituted with halo, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,1-dioxo-2,3,4,5-tetrahydroisothiazol-2-yl, or tetrazol-5-yl optionally substituted with  $C_1$ - $C_3$  alkyl;

30  $R^{16}$  is hydrogen, chloro, isobutyl,  $\text{CH}_2\text{R}^{24}$ ;  $\text{CF}_2\text{R}^{25}$ , 1,1,1-trifluoro-2-hydroxyeth-2-yl,  $\text{C}_2$ - $\text{C}_4$  alkenyl optionally substituted with one or two fluorine atoms,  $\text{OR}^{26}$ ,  $\text{C}(\text{O})\text{R}^{27}$ ,  $\text{N}(\text{methyl})(\text{methylsulfonyl})$ ,  $\text{N}(\text{methyl})(\text{acetyl})$ , pyrrolidin-2-on-1-yl, methylsulfonyl,  $\text{N},\text{N}$ -dimethylaminosulfonyl, phenyl optionally substituted with one or two substituents



selected from the group consisting of hydroxymethyl, methoxy, fluoro, and methylsulfonyl, 1,3-dioxolan-2-yl, 1,3-dithiolan-2-yl, 1,3-oxathiolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithian-2-yl, pyridinyl, thiazolyl, oxazolyl, or 1,2,4-oxadiazolyl optionally substituted with methyl;

- 5           R<sup>17</sup> is hydrogen or fluoro;  
          R<sup>18</sup> is ethynyl or cyclopropyl;  
          R<sup>19</sup> is hydrogen or methyl;  
          R<sup>20</sup> is difluoromethyl or methanesulfonyl;  
          R<sup>21</sup> is C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, phenyl, or -NR<sup>30</sup>R<sup>31</sup>;  
10          R<sup>22</sup> is hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl optionally substituted with up to 3 fluorine atoms, or C<sub>3</sub>-C<sub>6</sub> cycloalkyl;  
          R<sup>23</sup> is C<sub>1</sub>-C<sub>3</sub> alkyl or C<sub>3</sub>-C<sub>6</sub> cycloalkyl;  
          R<sup>24</sup> is fluoro, hydroxy, or C<sub>1</sub>-C<sub>3</sub> alkoxy;  
          R<sup>25</sup> is hydrogen, phenyl, or furyl;  
15          R<sup>26</sup> is C<sub>1</sub>-C<sub>3</sub> alkyl optionally substituted with one or two fluorine atoms;  
          R<sup>27</sup> is C<sub>1</sub>-C<sub>3</sub> alkyl, C<sub>3</sub>-C<sub>5</sub> cycloalkyl, C<sub>2</sub>-C<sub>3</sub> alkenyl, C<sub>1</sub>-C<sub>3</sub> alkoxy, NR<sup>28</sup>R<sup>29</sup>, pyrrolidin-1-yl optionally substituted with methyl or one or two fluorine atoms, piperidin-1-yl, phenyl, pyridinyl, or furyl;  
          R<sup>28</sup> is hydrogen or methyl;  
20          R<sup>29</sup> is methyl, ethyl, or propyl;  
          R<sup>30</sup> is hydrogen or methyl;  
          R<sup>31</sup> is methyl; or  
          R<sup>30</sup> and R<sup>31</sup> taken together with the nitrogen atom to which they are attached form a pyrrolidine or piperidine ring;  
25          R<sup>32</sup> is C<sub>1</sub>-C<sub>10</sub> alkyl optionally substituted with 1-6 fluorine atoms, oxo, or one or two hydroxy groups, C<sub>2</sub>-C<sub>6</sub> alkenyl, or -(CH<sub>2</sub>)<sub>0-3</sub>-R<sup>33</sup>;  
          R<sup>33</sup> is C<sub>3</sub>-C<sub>7</sub> cycloalkyl or phenyl each optionally substituted with one or two substituents independently selected from the group consisting of halo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, hydroxy, trifluoromethyl, and trifluoromethoxy, or R<sup>33</sup> is adamantyl;  
30          R<sup>34</sup> is hydrogen, R<sup>32</sup>, or -(CH<sub>2</sub>)<sub>0-2</sub>-OR<sup>32</sup>;  
          R<sup>35</sup> is hydroxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, or NR<sup>37</sup>R<sup>38</sup> where R<sup>37</sup> and R<sup>38</sup> are independently hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl, or R<sup>37</sup> and R<sup>38</sup>, taken together with the nitrogen to which they

are attached, form a piperidine ring optionally substituted with C<sub>1</sub>-C<sub>6</sub> alkyl, a homopiperidine ring, a morpholine ring, or a pyrrolidine ring optionally substituted with (C<sub>1</sub>-C<sub>6</sub> alkoxy)methyl;

R<sup>36</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl or adamantyl;

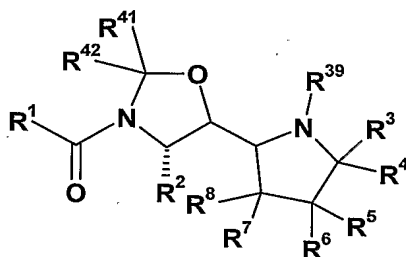
5 R<sup>39</sup> is hydrogen or a nitrogen protecting group;

R<sup>40</sup> is hydrogen or an oxygen protecting group;

or an acid addition salt thereof; provided that: a) no more than one of X, Y, and Q may be N or N<sup>+</sup>-O<sup>-</sup>; b) when X is CH, Y is CR<sup>16</sup>, and Q is CR<sup>17</sup>, then one of R<sup>16</sup> and R<sup>17</sup> is other than hydrogen; and c) at least one of R<sup>39</sup> and R<sup>40</sup> is other than hydrogen.

10

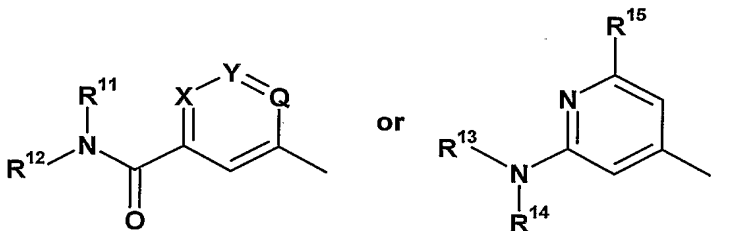
10. A compound of Formula IV:



IV

where:

15 R<sup>1</sup> is (C<sub>3</sub>-C<sub>7</sub> cycloalkyl)<sub>0-1</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), (C<sub>3</sub>-C<sub>7</sub> cycloalkyl)<sub>0-1</sub>(C<sub>2</sub>-C<sub>6</sub> alkenyl), (C<sub>3</sub>-C<sub>7</sub> cycloalkyl)<sub>0-1</sub>(C<sub>2</sub>-C<sub>6</sub> alkynyl) or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, each optionally substituted with up to three groups independently selected from halo, hydroxy, thiol, cyano, trifluoromethyl, trifluoromethoxy, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>3</sub>-C<sub>7</sub> cycloalkoxy, oxo, and NR<sup>9</sup>R<sup>10</sup>, hydrogen,



biphenyl substituted with halo,

20 X is CH, N, or N<sup>+</sup>-O<sup>-</sup>;

Y is CR<sup>16</sup>, N, or N<sup>+</sup>-O<sup>-</sup>;

Q is CR<sup>17</sup>, N, or N<sup>+</sup>-O<sup>-</sup>;

$R^2$  is  $C_1$ - $C_3$  alkyl, benzyl optionally monosubstituted in the phenyl ring with a substituent selected from the group consisting of halo,  $C_1$ - $C_6$  alkoxy optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, and  $C_1$ - $C_6$  alkylthio optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, or benzyl optionally disubstituted in the phenyl ring  
 5 with a first substituent independently selected from halo and a second substituent independently selected from halo,  $C_1$ - $C_6$  alkoxy optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, and  $C_1$ - $C_6$  alkylthio optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl;

$R^3$  is hydrogen or  $C_1$ - $C_6$  alkyl;

10  $R^4$  is hydrogen,  $C_1$ - $C_6$  alkyl, or phenyl;

$R^3$  and  $R^4$  taken together with the carbon to which they are attached form a  $C_3$ - $C_6$  cycloalkyl ring;

$R^5$  is hydrogen, fluoro, trifluoromethyl,  $R^{32}$ , or phenyl optionally monosubstituted with  $C_1$ - $C_6$  alkyl or  $C_1$ - $C_6$  alkoxy;

15  $R^6$  is fluoro, hydroxy, p-toluenesulfonyloxy,  $R^{34}$ ,  $-\text{CH}_2\text{C}(\text{O})\text{R}^{35}$ , or  $-\text{OC}(\text{O})\text{NHR}^{36}$ ; or  $R^5$  and  $R^6$  taken together form  $=\text{CHC}(\text{O})(\text{C}_1\text{-C}_4 \text{ alkoxy})$  or oxo;

$R^7$  is hydrogen or fluoro; or  $R^6$  and  $R^7$  taken together form a bond;

$R^8$  is hydrogen or fluoro;

$R^9$  is hydrogen,  $C_1$ - $C_6$  alkyl, or phenyl;

20  $R^{10}$  is hydrogen,  $C_1$ - $C_6$  alkyl, phenyl,  $-\text{C}(\text{O})(\text{C}_1\text{-C}_6 \text{ alkyl})$ , or  $-\text{SO}_2(\text{C}_1\text{-C}_6 \text{ alkyl})$ ;

$R^{11}$  and  $R^{12}$  are independently selected from the group consisting of methyl, ethyl, and propyl;

$R^{13}$  is hydrogen or  $C_1$ - $C_6$  alkyl;

$R^{14}$  is  $C_3$ - $C_5$  cycloalkyl,  $C_1$ - $C_6$  alkyl, or  $-\text{CH}_2\text{R}^{18}$ ;

25  $R^{15}$  is  $-\text{CF}_2\text{R}^{19}$ ,  $-\text{OR}^{20}$ ,  $-\text{CH}_2\text{C}(\text{O})\text{CH}_3$ ,  $-\text{S}(\text{O})_{1-2}\text{R}^{21}$ ,  $-\text{NR}^{22}\text{SO}_2\text{R}^{23}$ ,  $(\text{C}_1\text{-C}_3 \text{ alkoxy})$ -carbonyl, phenyl optionally substituted with halo, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,1-dioxo-2,3,4,5-tetrahydroisothiazol-2-yl, or tetrazol-5-yl optionally substituted with  $C_1$ - $C_3$  alkyl;

30  $R^{16}$  is hydrogen, chloro, isobutyl,  $\text{CH}_2\text{R}^{24}$ ,  $\text{CF}_2\text{R}^{25}$ , 1,1,1-trifluoro-2-hydroxyeth-2-yl,  $\text{C}_2$ - $\text{C}_4$  alkenyl optionally substituted with one or two fluorine atoms,  $\text{OR}^{26}$ ,  $\text{C}(\text{O})\text{R}^{27}$ , N(methyl)(methylsulfonyl), N(methyl)(acetyl), pyrrolidin-2-on-1-yl, methylsulfonyl, N,N-dimethylaminosulfonyl, phenyl optionally substituted with one or two substituents

selected from the group consisting of hydroxymethyl, methoxy, fluoro, and methylsulfonyl, 1,3-dioxolan-2-yl, 1,3-dithiolan-2-yl, 1,3-oxathiolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithian-2-yl, pyridinyl, thiazolyl, oxazolyl, or 1,2,4-oxadiazolyl optionally substituted with methyl;

5         $R^{17}$  is hydrogen or fluoro;

$R^{18}$  is ethynyl or cyclopropyl;

$R^{19}$  is hydrogen or methyl;

$R^{20}$  is difluoromethyl or methanesulfonyl;

$R^{21}$  is  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  cycloalkyl, phenyl, or  $-NR^{30}R^{31}$ ;

10         $R^{22}$  is hydrogen,  $C_1$ - $C_3$  alkyl optionally substituted with up to 3 fluorine atoms, or  $C_3$ - $C_6$  cycloalkyl;

$R^{23}$  is  $C_1$ - $C_3$  alkyl or  $C_3$ - $C_6$  cycloalkyl;

$R^{24}$  is fluoro, hydroxy, or  $C_1$ - $C_3$  alkoxy;

$R^{25}$  is hydrogen, phenyl, or furyl;

15         $R^{26}$  is  $C_1$ - $C_3$  alkyl optionally substituted with one or two fluorine atoms;

$R^{27}$  is  $C_1$ - $C_3$  alkyl,  $C_3$ - $C_5$  cycloalkyl,  $C_2$ - $C_3$  alkenyl,  $C_1$ - $C_3$  alkoxy,  $NR^{28}R^{29}$ , pyrrolidin-1-yl optionally substituted with methyl or one or two fluorine atoms, piperidin-1-yl, phenyl, pyridinyl, or furyl;

$R^{28}$  is hydrogen or methyl;

20         $R^{29}$  is methyl, ethyl, or propyl;

$R^{30}$  is hydrogen or methyl;

$R^{31}$  is methyl; or

$R^{30}$  and  $R^{31}$  taken together with the nitrogen atom to which they are attached form a pyrrolidine or piperidine ring;

25         $R^{32}$  is  $C_1$ - $C_{10}$  alkyl optionally substituted with 1-6 fluorine atoms, oxo, or 1 or 2 hydroxy groups,  $C_2$ - $C_6$  alkenyl, or  $-(CH_2)_{0-3}-R^{33}$ ;

$R^{33}$  is  $C_3$ - $C_7$  cycloalkyl or phenyl each optionally substituted with one or two substituents independently selected from the group consisting of halo,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, hydroxy, trifluoromethyl, and trifluoromethoxy, or  $R^{33}$  is adamantyl;

30         $R^{34}$  is hydrogen,  $R^{32}$ , or  $-(CH_2)_{0-2}-OR^{32}$ ;

$R^{35}$  is hydroxy,  $C_1$ - $C_6$  alkoxy, or  $NR^{37}R^{38}$  where  $R^{37}$  and  $R^{38}$  are independently hydrogen or  $C_1$ - $C_6$  alkyl, or  $R^{37}$  and  $R^{38}$ , taken together with the nitrogen to which they

are attached, form a piperidine ring optionally substituted with C<sub>1</sub>-C<sub>6</sub> alkyl, a homopiperidine ring, a morpholine ring, or a pyrrolidine ring optionally substituted with (C<sub>1</sub>-C<sub>6</sub> alkoxy)methyl;

R<sup>36</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl or adamantyl;

5 R<sup>39</sup> is hydrogen or a nitrogen protecting group;

R<sup>41</sup> and R<sup>42</sup> are independently selected from methyl, ethyl, and propyl;

or an acid addition salt thereof; provided that no more than one of X, Y, and Q may be N or N<sup>+</sup>-O<sup>-</sup>.